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Synthesis of novel dansyl appended cyclodextrins. Self-inclusion and sensor properties

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The synthesis of three dansyl appended cyclodextrin derivatives, differing in the spacer length between cyclodextrin and the dansyl moiety, is described. In compound 4 the fluorophore is directly attached to the cyclodextrin. Compound 5 contains an ethyl spacer and compound 6 a triethylene glycol spacer. These compounds are designed to detect neutral organic guest molecules like cyclohexanol and adamantanecarboxylic acid in water by fluorescence spectroscopy. At neutral pH none of the compounds is sensitive towards guest molecules. For compound 4 this is due to the fact that the dansyl group is located outside the cyclodextrin cavity. For compunds 5 and 6 the low sensitivity is the result of a strong self-inclusion of the dansyl group. Lowering the pH results in protonation of the dimethylamino group of the dansyl moiety, which makes the self-inclusion less favourable leading to a strongly increased response towards guests. This phenomenon allows the sensors to be switched on and off by lowering or increasing the pH of the solution. Compound 6 is able to detect adamantanecarboxylic acid at 5×10^{-7} mol^{-1} dm^3 concentration at pH 1.

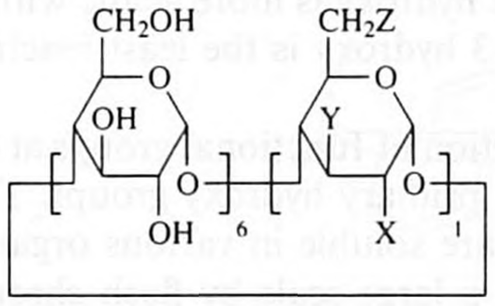
Introduction

Cyclodextrins (CDs) are a group of naturally occurring cyclic oligomers of D-glucose, which are soluble in water and contain a hydrophobic cavity. In aqueous solution they are able to form inclusion (host–guest) complexes with a wide variety of organic compounds.[1] As CDs are spectroscopically rather inert, inclusion phenomena involving these molecules are usually studied with spectroscopically active guest molecules. Upon modification with chromophoric groups, CDs can be converted into spectroscopically active species, which can be used to bind guest molecules that cannot be detected easily by spectroscopic methods themselves. Applying these CD derivatives to the detection of organic compounds in aqueous media is of great interest since this would, for example, provide the possibility of detecting low levels of organic pollutants in water.

The mechanism for such a sensor system is shown in Fig. 1. Initially, the chromophore is intramolecularly bound into the cavity of the CD, as was recently confirmed for a CD derivative, modified at C-6 with *N*-dansylethylenediamine, by Corradini *et al.*[2] by performing ^{1}H NMR ROESY experiments. Binding of a guest molecule will lead to the exclusion of the chromophore from the hydrophobic cavity into the polar aqueous solution. The binding thus results in a dramatic environmental change of the chromophoric group with concomitant changes in spectroscopic properties.

Various CD derivatives with covalently linked chromophoric groups have been made which show guest-induced variations in their absorption[3] or circular dichroic spectra.[4] Modification with fluorophores, however, leads to more sensitive sensor systems, since fluorescence experiments can be conducted at much lower concentrations.[5] Among fluorophores whose emissions are sensitive to the environment the dansyl (5-dimethylamino-1-naphthylsulfonyl) group has shown great promise.[6] In a polar solvent, such as water, the fluorescence emission of the dansyl group is relatively weak, whereas in non-polar solvents the emission intensity is higher and the emission wavelength is blue shifted.

With this in mind Ueno *et al.*[6] prepared a number of dansyl appended cyclodextrins, among which a set of three related compounds, **1**, **2** and **3**,[6d] functionalised at C-2, C-3 and C-6



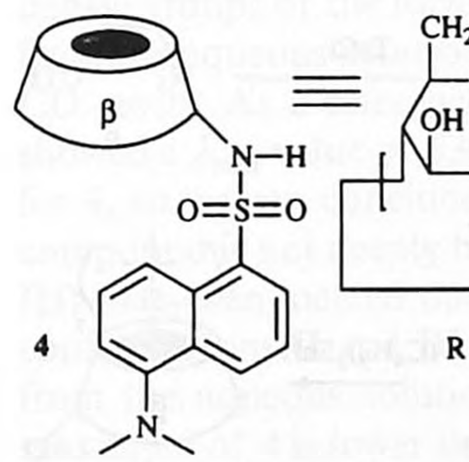
1 : X = O-dansyl, Y = OH, Z = OH

2 : X = OH, Y = O-dansyl, Z = OH

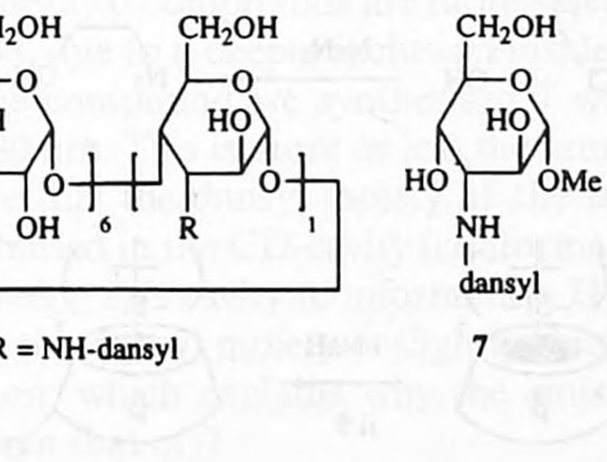
3 : X = OH, Y = OH, Z = O-dansyl

respectively with dansyl esters. Upon addition of guest, only **1** and **3** showed guest-induced changes in emission spectra. Compound **2** could not be used as a sensor because of a very tight binding of the dansyl group in the CD cavity, as was concluded from time-resolved fluorescence experiments and CPK models.[6d] Comparison of results for different guests showed that the C-2 functionalised compound **1** is a much better sensor than the C-6 derivative **3**. Although both compounds give good results they lack sufficient stability for a good sensor device since the ester bonds are vulnerable to the action of acid and base.

In this paper we wish to report on three new dansyl functionalised CDs, **4**, **5** and **6**, which contain ether and amide linkages

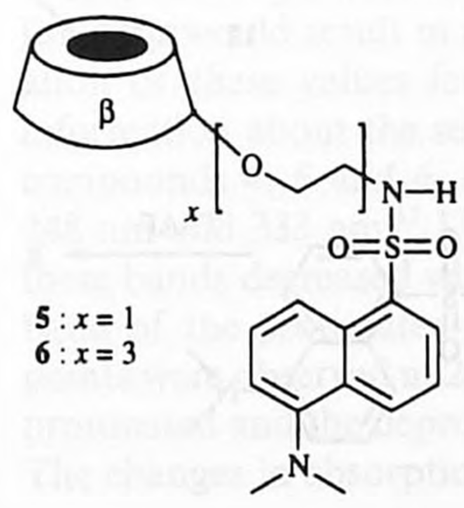


4



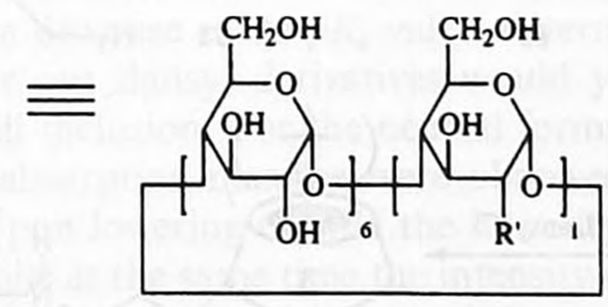
R = NH-dansyl

7



5 : $x = 1$

6 : $x = 3$



R' = $(O\text{-}CH_2\text{-}CH_2)_x$-NH-dansyl

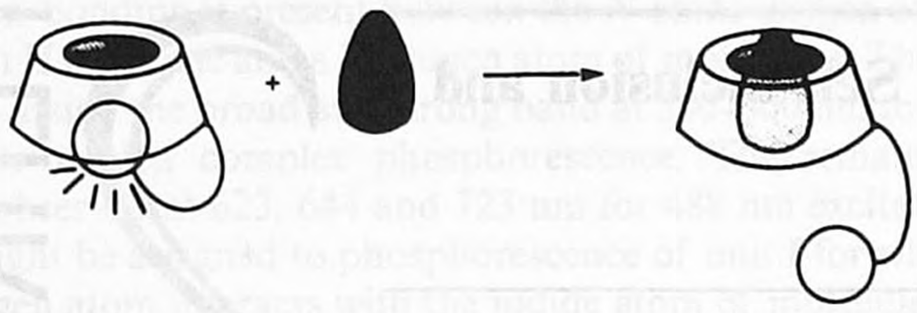


Fig. 1 Schematic representation of the sensor mechanism

instead of labile ester bonds to secure stability towards acid and base. All three compounds are modified at secondary positions, since this gives the best results according to literature.[6] By lengthening of the linking spacer from **4** to **6**, the fluorophore might have more freedom to move away from the cavity when it is excluded by a guest. This might lead to a more dramatic change in the polarity of the environment and give rise to larger changes in emission intensity, resulting in an increased sensitivity. A polar oligoethylene glycol spacer is chosen for **6** rather than an alkyl chain, since the latter can be included in the CD cavity, as was observed by us for alkyl spacers in CD dimers.[7]

Results and discussion

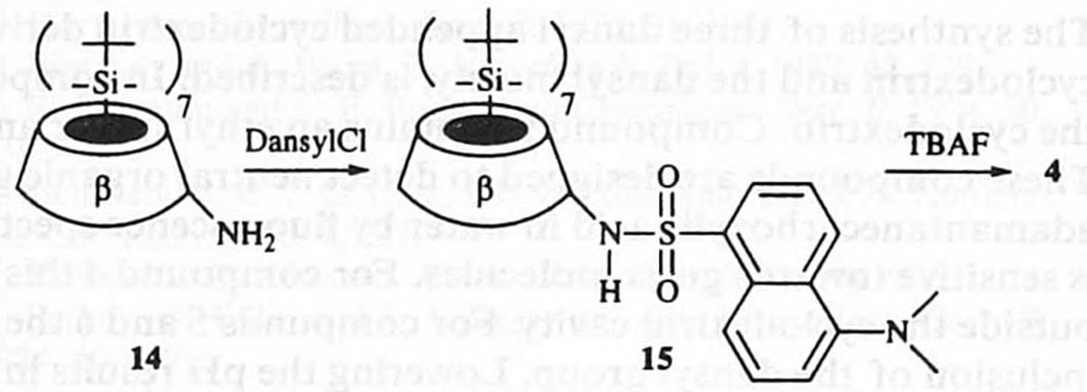
Modified cyclodextrins

The synthesis of modified cyclodextrins **4**, **5** and **6** is possible by making use of the differences in reactivity of the three types of hydroxy groups present in these molecules. The C-6 hydroxys, being primary alcohols, are more nucleophilic compared to the C-2 and C-3 hydroxys which are secondary alcohols. The two types of secondary hydroxys have different reactivities due to a difference in pK_a value.[8] The C-2 hydroxy is more acidic with a pK_a value of 12.1,[9] while the C-3 hydroxy is the least reactive substituent.

The first step towards introduction of functional groups at C-2 and C-3 is the silylation of all primary hydroxy groups. The resulting silylated cyclodextrins are soluble in various organic solvents and can be purified on a large scale by flash chromatography.[7,10,11] The next step is the selective deprotonation of the C-2-OH with a base resulting in an alkoxy anion which can be directly reacted with electrophiles.[10] When reacted with tosyl chloride, the resulting tosylate can be converted to its corresponding epoxide by an intramolecular reaction with an adjacent C-3 hydroxy. Opening of this epoxide by a nucleophile offers an alternative route for introduction of functional groups. The latter procedure, however, results in the conversion of one glucose unit into an altrose unit and the functionalisation occurring at C-2 instead of C-2.[7,10]

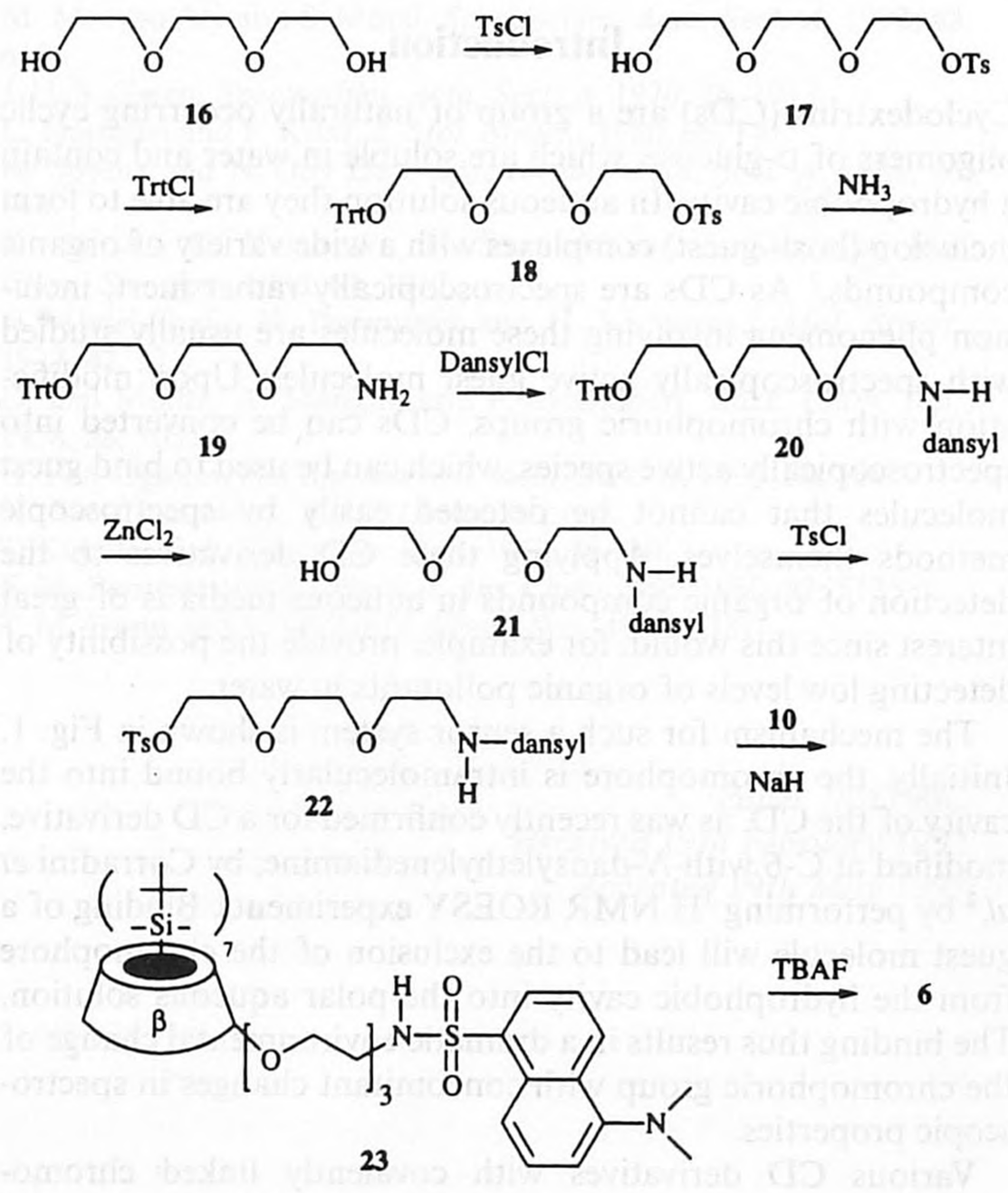
The synthesis of **5** started with 2-chloroethanol, which was converted into **8** by reaction with sodium azide (50% yield, Scheme 1). The resulting alcohol was tosylated in pyridine to give compound **9** in 32% yield. Compound **10** was deprotonated at C-2 with sodium hydride and subsequently reacted with **9** to give the azide-functionalised cyclodextrin **11** in 27% yield after purification by repeated column chromatography. This yield is quite good considering the formation of a statistical mixture of non, singly and doubly reacted compounds. We found that the deprotonated cyclodextrin **10** only reacted with tosylated alkyl groups and not with alkyl halides. The azide group of **11** was reduced with tri-*n*-butyltin hydride in the presence of 2,2′-azoisobutyronitrile (AIBN). The resulting amine was reacted with dansyl chloride to give **13** in 58% yield.

A similar procedure was followed for the synthesis of **4**, which was carried out by reacting dansyl chloride with the monofunctionalised CD **14**. The latter compound was synthesised according to a procedure described previously (Scheme 2).[7]



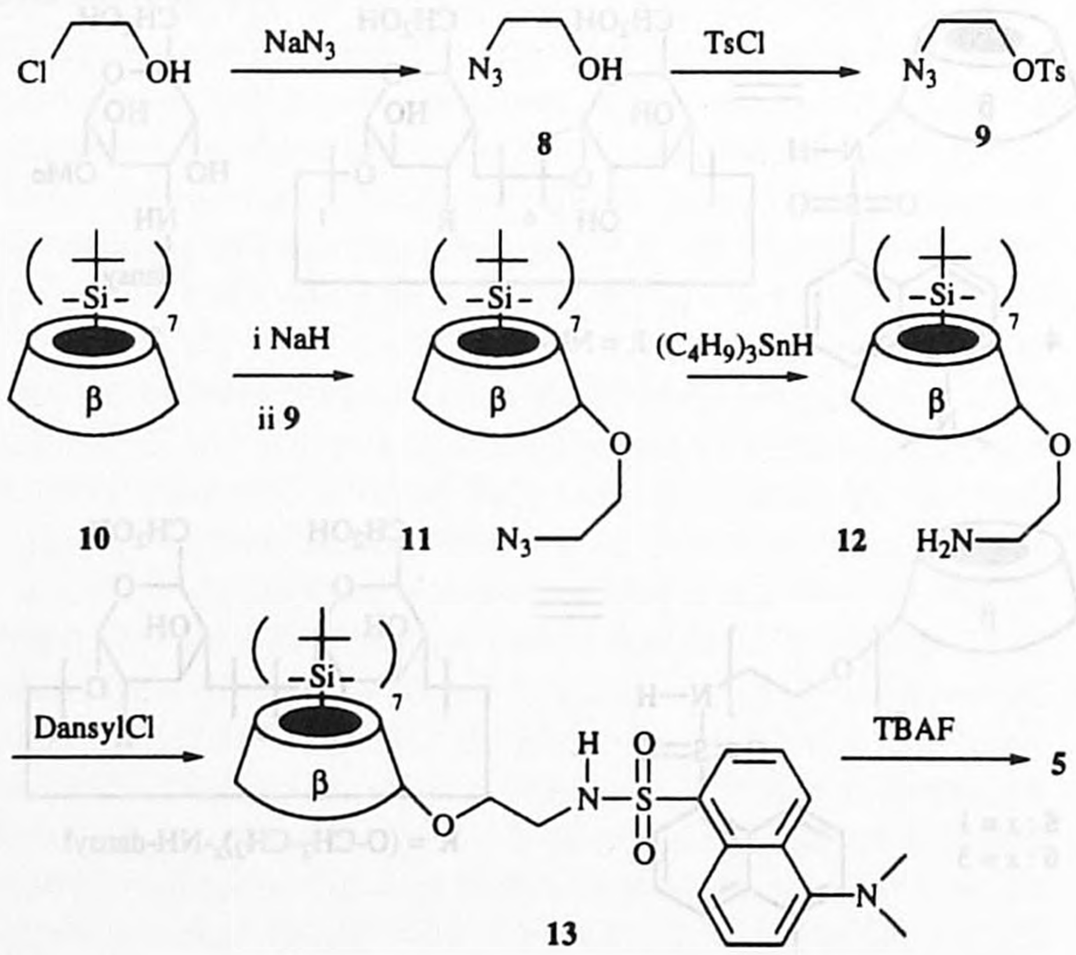
Scheme 2 Synthesis of **4**

To obtain compound **6**, triethylene glycol **16** was monotosylated using NaH as a base giving **17** in 80% yield (Scheme 3).



Scheme 3 Synthesis of **6**

The remaining hydroxy function was subsequently protected with a triphenylmethyl (Trt) group. The protected compound **18** was treated with ammonia gas dissolved in ethanol, using an autoclave, to give amine **19** in 72% yield. The latter compound was coupled to dansyl chloride and the resulting compound **20** was deprotected with $ZnCl_2$ in dichloromethane–methanol giving **21** in 72% yield. Tosylation (66% yield) with tosyl chloride in pyridine yielded **22** as a yellow oil. The silylated cyclodextrin **10** was deprotonated with sodium hydride in refluxing tetrahydrofuran (THF) and the resulting alkoxide reacted with 0.6 equiv. of **22** to give compound **23** in 33% yield after column chromatography.



Scheme 1 Synthesis of **5**

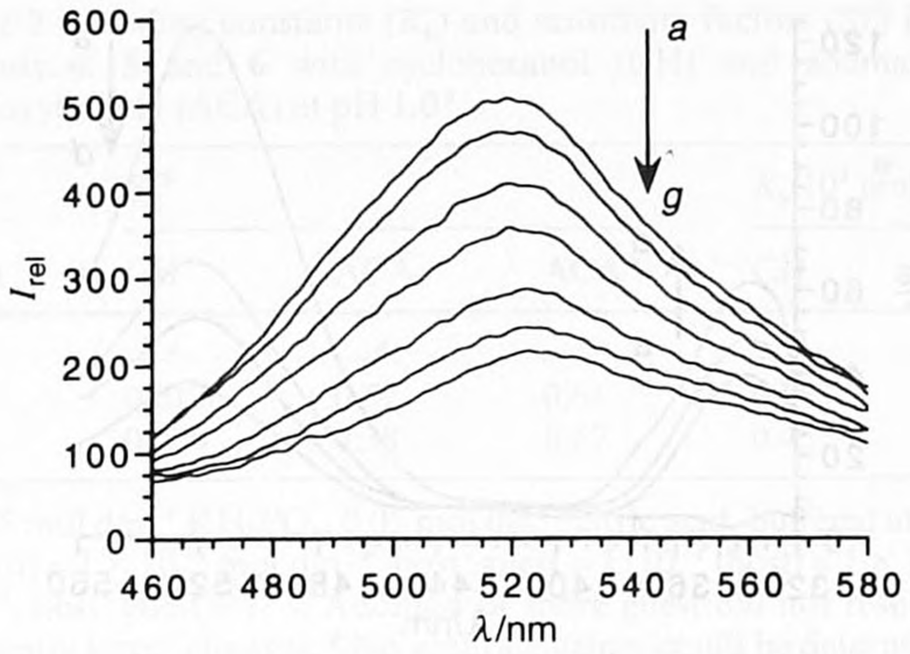


Fig. 2 Changes in the emission spectrum of **5** (1.0×10^{-5} mol dm^{-3}, λ_{exc} 305 nm) in water of pH 1.0 upon addition of adamantane-1-carboxylic acid (ACA). (*a*) [ACA] = 0; (*b*) [ACA] = 1.0×10^{-6}; (*c*) [ACA] = 3.3×10^{-6}; (*d*) [ACA] = 6.3×10^{-6}; (*e*) [ACA] = 1.2×10^{-5}; (*f*) [ACA] = 1.7×10^{-5}; (*g*) [ACA] = 2.7×10^{-5} mol dm^{-3}.

Table 1 Binding constants (K_b) and sensitivity factors (*Sf*) for compounds **4**, **5** and **6** with cyclohexanol (CH) and adamantane-1-carboxylic acid (ACA) at pH 7.0[a]

	Sf[b]		K_b/10^3 mol^{-1} dm^3	
Host	CH	ACA	CH	ACA
4	—[c]	—[c]	—[c]	—[c]
5	0.0001	0.003	0.02	10.4
6	0.0006	0.022	0.07	6.3

[a] 0.1 mol dm^{-3} KH_2PO_4 buffered at pH 7.0. [b] [host] = 1×10^{-6} mol dm^{-3}; host : guest = 1 : 10. [c] No accurate values could be determined.

Desilylation of the protected intermediates **15**, **13** and **23** by tetrabutylammonium fluoride (TBAF) in refluxing THF finally yielded the desired products **4**, **5** and **6** in 63, 76 and 79% yields, respectively. The compounds were purified by dissolving them in a small volume of ethanol–water (2 : 1, v/v) followed by precipitation with ethyl acetate. Removal of the last traces of the TBA salts was achieved using either cation-exchange chromatography or exclusion chromatograhy. All three compounds were fully characterised by elemental analysis and spectroscopic methods.

Sensor properties at pH 7.0

Compounds **4**, **5**, **6** were studied with respect to their ability to detect the guest compounds adamantane-1-carboxylic acid (ACA) and cyclohexanol (CH) in water at pH 7.0. The emission spectra of the host compounds were recorded at various concentrations of ACA and CH. Addition of the guest resulted in a decrease of the fluorescence intensity, which is an indication for the exclusion of the dansyl group from the cyclodextrin cavity (Fig. 2). This guest-induced variation of the emission intensity was used to determine binding constants (Table 1).

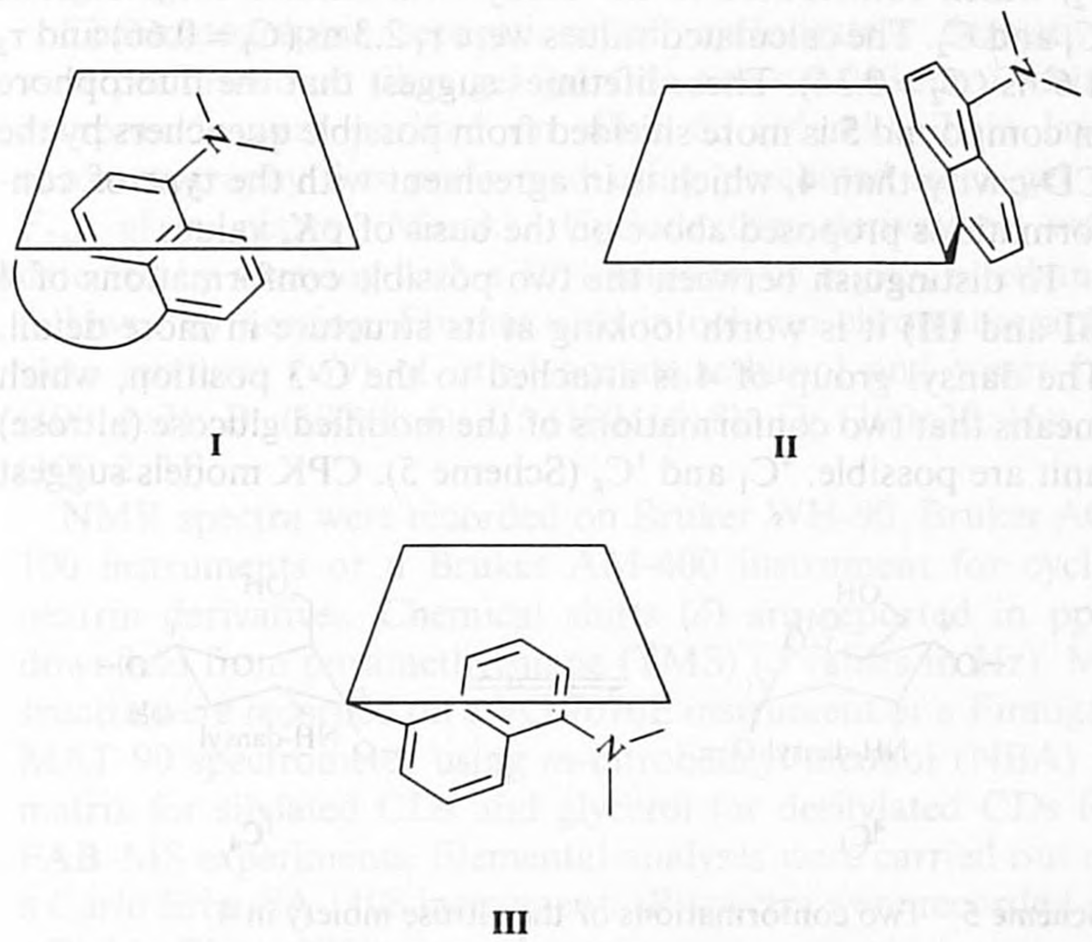
To further characterise the binding of guest molecules by this class of compounds, Ueno *et al.*[6a] introduced a sensitivity or response factor (*Sf*), which describes the suitability of the sensor molecule to detect a certain guest. This *Sf* is defined as in eqn. (*a*), in which I_0 is the emission intensity in absence of any

$$Sf = \Delta I/I_0 \qquad (a)$$

guest and ΔI is the change in intensity of the observed fluorescence signal ($I - I_0$) at a certain host–guest ratio (*e.g.* 1 : 10). It is worth mentioning that comparison of *Sf* values from different publications is not always feasible, since their sizes depend on the host–guest ratio and the concentration of the sensor compound. We determined *Sf* values at a host concentration of 1×10^{-6} mol dm^{-3} and a host : guest ratio of 1 : 10. The results are summarised in Table 1.

The *Sf* values of **5** and **6** were smaller than we expected on the basis of values reported by Ueno,[6d] who found values of 0.04 (CH) and 0.65 (ACA) for the related compound **1**. These values, however, were determined at a higher host concentration (1×10^{-5} mol dm^{-3}) and can, therefore, not completely be compared with our values. The binding constants can be compared, but they are also significantly smaller than those found by Ueno,[6d] 0.58×10^3 mol^{-1} dm^3 for CH and 28.1×10^3 mol^{-1} dm^3 for ACA. These differences could be the result of a strong inclusion of the dansyl unit in the CD cavity in our case, which is possible due to the presence of a spacer between the fluorophore and the cyclodextrin.

For compound **4** the changes in emission intensity were too small to calculate accurate *Sf* factors and binding constants. This indicates that the environment of the dansyl group in this host molecule does not change significantly. This may be caused by a very strong self-inclusion as in conformation **I** (Scheme 4)



I **II** **III**

Scheme 4 Three possible conformations of the dansyl moiety

or it may be the result of the fact that the dansyl group is not included in the CD cavity at all as depicted for conformation **II**.

Self-inclusion

Since the self-inclusion is a major part of the sensor mechanism, we investigated it in more detail by comparison of the maximum emission wavelengths (λ_{max} value) of compounds **4**, **5** and **6**. These are lower for compounds **5** (519 nm) and **6** (520 nm) than for compound **4** (526 nm), which indicates that the dansyl groups of the former two compounds are more shielded from the aqueous solution, due to a deeper inclusion inside the CD cavity. As a reference compound we synthesised **7** which showed a λ_{max} value of 530 nm. This is more or less the same as for **4**, so we can conclude that the dansyl moiety of the latter compound is not deeply buried in the CD-cavity (conformation **III**) or is even located outside this cavity (conformation **II**). In conformations **II** and **III** the dansyl moiety is slightly shielded from the aqueous solution, which explains why the emission maximum of **4** is lower than that of **7**.

Since we expected that the inclusion of the dimethylamino function would result in a decrease of its pK_a value, determination of these values for our dansyl derivatives would yield information about the self-inclusion. For the neutral forms of compounds **4**, **5** and **6**, absorption maxima were observed at 248 nm and 333 nm.[12] Upon lowering the pH the intensity of these bands decreased while at the same time the intensity of a band of the protonated form at 286 nm increased. Isosbestic points were observed at 231, 268 and 306 nm indicating that the protonated and the deprotonated forms interconverted directly. The changes in absorption at 286 and 333 nm as a function of

pH were used to calculate the pK_a values. Compound **4** showed a pK_a value of 4.0, which is similar to the reported value of free dansylamide.[12] This confirms our conclusion that the dimethylamino moiety of **4** is either partly included in the CD-cavity as in conformation **III** (Scheme 4) or located outside the cavity (conformation **II**). The pK_a values of compounds **5** and **6**, 1.5 and 2.5 respectively, are significantly smaller than the pK_a values of **4**. This suggests that the dimethylamino units of compounds **5** and **6** are completely encapsulated by the CD-ring (conformation **I**), in contrast with that of **4**.

To further investigate the self-complexation behaviour we determined the fluorescence lifetimes of compounds **4** and **5** at pH 7.0 using the picosecond single photon count (SPC) technique.[13] The lifetime (τ) for compound **5** could be obtained by a mono-exponential fitting of the fluorescence decay curve which gave a value of 8.3 ns. For compound **4** the fluorescence decay could be analysed by assuming two lifetime components (τ_1 and τ_2) which contributed to the decay with relative contributions C_1 and C_2. The calculated values were τ_1 2.3 ns ($C_1 = 0.66$) and τ_2 4.6 ns ($C_2 = 0.34$). These lifetimes suggest that the fluorophore in compound **5** is more shielded from possible quenchers by the CD-cavity than **4**, which is in agreement with the type of conformations proposed above on the basis of pK_a values.

To distinguish between the two possible conformations of **4** (**II** and **III**) it is worth looking at its structure in more detail. The dansyl group of **4** is attached to the C-3 position, which means that two conformations of the modified glucose (altrose) unit are possible: $^4C_1$ and $^1C_4$ (Scheme 5). CPK models suggest

$^4C_1$ $^1C_4$

Scheme 5 Two conformations of the altrose moiety in **4**

that in the case of a $^4C_1$-conformation the dansyl group can be encapsulated by the CD-unit, yielding a type **III** conformation, but not in the case of a $^1C_4$-conformation. In the former conformation the dansyl group is in an axial position, which is energetically unfavourable. The energy required to attain this conformation, however, could be provided by the self-inclusion process. The J_{12} coupling constant in the 400 MHz ^{1}H NMR spectrum of **4** in D_2O amounted to 6.1 Hz, which is in accordance with a diaxial coupling, indicating a $^1C_4$-conformation which makes the existence of a type **III** conformation unlikely.

More evidence for a type **II** conformation was an upfield shift of 0.46 ppm to δ 4.4 of one of the H-1 signals, which are located at the outside of the CD-ring. It is known from the literature[14] that binding of an aromatic guest inside the cavity results in shifts of the H-3 and H-5 protons, which are located at the inside of the CD-ring. This suggests that the dansyl group of **4** is located outside the CD-cavity, in close proximity to one of the H-1 protons, which is in agreement with a type **II** conformation. The peak at δ 4.4 moved to lower field upon heating, suggesting the existence of another type **II** conformation in which the shielding by the dansyl moiety is less effective since its rotation away from the H-1 site is made easier at high temperature. The existence of two such type **II** conformations might explain the two lifetime components which were necessary to describe the fluorescence decay of compound **4**. These also indicate that the dansyl group has two different geometries in the $^1C_4$-conformation, differing from each other in the amount of shielding of the fluorophore from possible quenchers. In one type **II** conformation the dansyl moiety might be close to the wall of the CD ring and is shielded by it from quenchers, while in the other the fluorophore might be rotated away from the CD wall and is less shielded.

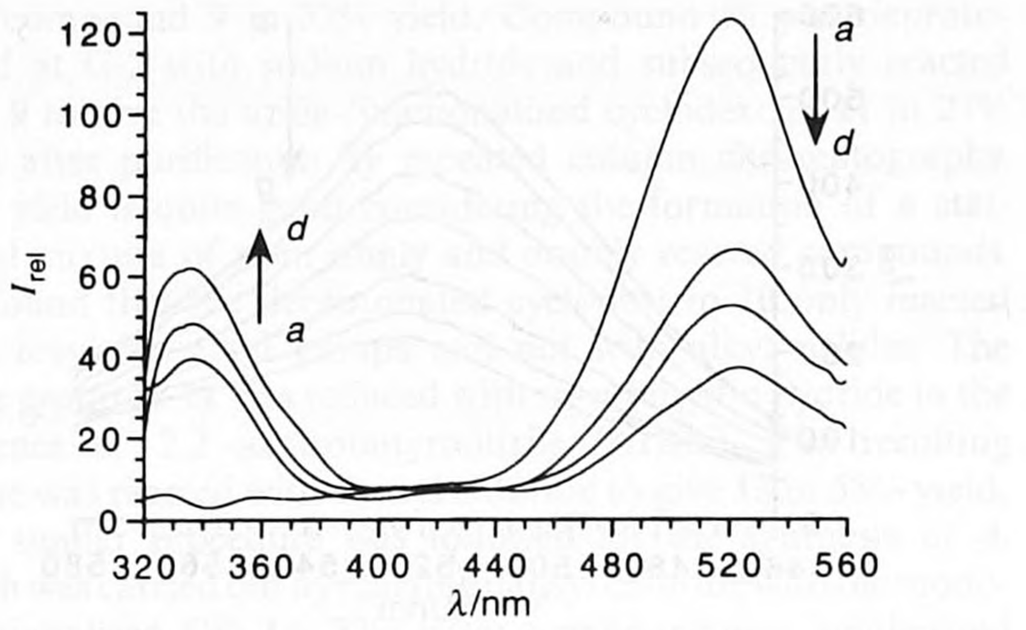


Fig. 3 Corrected emission spectra of **6** (1×10^{-5} mol dm^{-3}, λ_{exc} 305 nm) in water of different pH values; (*a*) pH 3.89; (*b*) pH 2.51; (*c*) pH 1.92; (*d*) pH 0.58

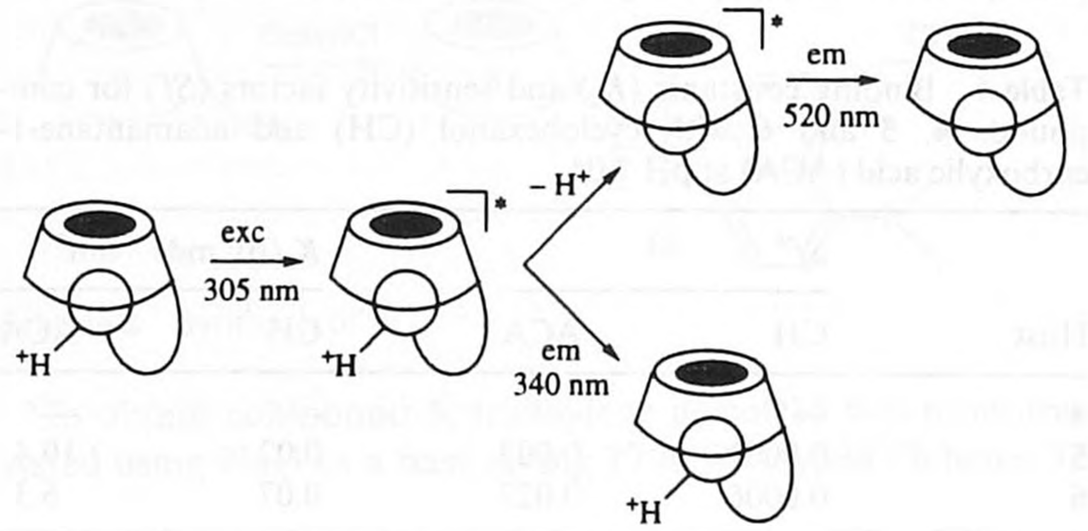


Fig. 4 Excited state proton transfer

Sensor properties at pH 1.0

As shown above (Table 1) sensor molecules **5** and **6** have very low *Sf* values as a result of the tight binding of the dansyl moiety inside the CD cavity. To overcome this problem, we decided to lower the pH of the solution which leads to the protonation of the dansyl group and is expected to result in a less tight self-inclusion of this group, and hence to a better response towards guest molecules.

Since it is known that pyrene-appended CDs can dimerise in solution[15] we first investigated whether our host molecules formed dimers or aggregates in water at higher concentrations. All three compounds showed a linear increase in emission intensity as a function of concentration (1×10^{-7} to 1×10^{-5} at pH 1.0 and 1×10^{-7} to 2×10^{-6} mol dm^{-3} at pH 7.0), indicating that no aggregation occurred under these conditions. At concentrations above 3×10^{-5} mol dm^{-3} at pH 1.0 deviations from linearity were observed for compounds **4** and **6** due to inner filter effects. For compound **5** this deviation was already observed above concentrations of 1×10^{-5} mol dm^{-3} at pH 1.0, probably due to the higher fluorescent quantum yield of this compound.

In the fluorescence spectrum of compound **6** at pH 0.6 two emission bands are present which can be ascribed to the protonated (335 nm) and the deprotonated (520 nm) form (Fig. 3).[12] According to the UV–VIS spectrum all molecules are protonated at pH 0.6. The fluorescence emission at 520 nm, therefore, must be the result of an excited state proton transfer equilibrium, due to a decrease in pK_a value in the excited state (pK_a*). This means that excitation of compound **6** at pH 0.6 will lead to partial deprotonation of the fluorophore, resulting in an emission signal of the neutral form at 520 nm (Fig. 4).

Binding studies were performed with compounds **4**, **5** and **6**, and the guests CH and ACA at pH = 1.0. The fluorescence band at 335 nm increased upon guest binding, whereas the band at 520 nm decreased. Apparently, binding favoured the formation of the protonated form of the CD-derivative, from which we may conclude that the deprotonated form is stabilised by self-complexation. Since the intensity decrease at 520 nm was

Table 2 Binding constants (K_b) and sensitivity factors (Sf) for compounds **4**, **5** and **6** with cyclohexanol (CH) and adamantane-1-carboxylic acid (ACA) at pH 1.0[a]

	Sf[b]			$K_b/10^3$ mol^{-1} dm^3	
Host	CH	ACA	ACA[c]	CH	ACA
4	—[d]	—[d]	—[d]	—[d]	—[d]
5	0.017	0.52	0.61	0.54	450
6	0.020	0.38	0.57	0.45	220

[a] 0.05 mol dm^{-3} KH_2PO_4, 0.05 mol dm^{-3} citric acid, buffered at pH 1.0. [b] [host] = 1×10^{-6} mol dm^{-3}, host : guest = 1 : 10. [c] [host] = 1×10^{-5} mol dm^{-3}, host : guest = 1 : 3. Addition of more guest did not result in significantly larger changes. [d] No accurate values could be determined.

larger than the intensity increase at 335 nm, the band at the former wavelength was used to calculate binding constants and Sf values. The results are summarised in Table 2. As can be concluded from this Table, compound **4** does not show any changes in fluorescence signals at pH = 1.0. This result is in agreement with the conclusion above that the dansyl group is located outside the CD cavity.

Both CH and ACA are detected by compounds **5** and **6** with much higher Sf values at pH 1.0 than at pH 7.0. The Sf values at low pH are in the same range as the values reported by Ueno.[6d] This comparison is not totally valid for the substrate ACA since our experiments were performed at lower pH (1.0) than those in the literature (7.0) and ACA, with a pK_a of 4.9,[16] is known to bind much more strongly at pH < 4.9 than at pH > 4.9.[16] Our Sf values, however, were determined at a lower host : guest ratio (1 : 3), which allows us to conclude that we have realised a very sensitive system. As few as 0.5 equiv. of ACA, which corresponds to a concentration of 5×10^{-7} mol dm^{-3}, results in a 10% fluorescence change.

The idea of using a longer spacer, as in compound **6**, was to increase the guest-induced changes in the fluorescence intensity. Since the Sf values of **6** for CH and ACA are the same, within experimental error, as those of **5**, we cannot conclude that a longer spacer has a positive effect. This might be due to the fact that the ethylene glycol chain still can be encapsulated in the cavity of **6**,[17] and thereby block the cavity for complexation of the guest molecule. We, however, have not investigated this in further detail.

Conclusions

The cyclodextrin derivatives described in this paper were designed to detect neutral organic guest molecules, like cyclohexanol and adamantanecarboxylic acid, by fluorescence spectroscopy. At neutral pH cyclodextrins **5** and **6** are not sensitive towards guest molecules as a result of a strong self-inclusion of the fluorophore attached to these molecules. In compound **4** the poor sensor properties are due to the fact that its dansyl moiety is located outside the cavity. The introduction of a spacer apparently allows the dansyl group to adopt an ideal conformation for self-inclusion.

By lowering the pH, however, we have succeeded in reaching Sf values that are comparable with values displayed by compounds described in the literature. Varying the pH, therefore, creates a tool to tune the self-inclusion of the dansyl moiety and thereby switching on and off the sensitivity of the sensor compounds towards guests. Compound **6** is able to detect concentrations of adamantanecarboxylic acid as low as 5×10^{-7} mol dm^{-3}, a value that has not yet been achieved with other cyclodextrin-based sensor molecules.

Although our compounds have the disadvantage that they only show high responses at low pH, their stabilities in aqueous solutions are much higher than those of **1**, **2** and **3**. This allows the use of our compounds in other detection formats like sol–gel matrices.[18] The design of novel sensor systems clearly is difficult and the following points have to be considered. The fluorophore should be able to form a self-inclusion complex with the CD-unit. The linking spacer must have a well-defined length and a rigidity such that the self-inclusion process is not favoured too much. For future applications it may be of interest to test more hydrophilic polarity probes which can make the self-inclusion a more balanced process.

Experimental

General

THF was distilled from sodium and benzophenone. Ethyl acetate was distilled *in vacuo*. Pyridine was dried by refluxing for at least 8 h over CaH_2 (5 g l^{-1}) followed by distillation. Methanol was dried by refluxing for at least 8 h over magnesium (activated by a little iodine) followed by distillation. All dry solvents were kept over molecular sieves (3 Å). All other reagents were of reagent grade and used without further purification.

Chromatographic separations of cyclodextrin derivatives were performed on silica gel (particle size < 0.063 mm). Other compounds were purified on silica 60 (Merck). Thin layer chromatography was performed using precoated silica gel 60 F_{254} glass plates (Merck). Cyclodextrin derivatives were detected by spraying with a 10% solution of H_2SO_4 in ethanol followed by heating. Eluents used in column chromatography were mixtures (v/v) of ethyl acetate, ethanol and water [A: (100 : 4 : 2); B: (100 : 8 : 4); C: (100 : 14 : 8); D: (100 : 30 : 16); E: (100 : 2 : 1)].

NMR spectra were recorded on Bruker WH-90, Bruker AC-100 instruments or a Bruker AM-400 instrument for cyclodextrin derivatives. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane (TMS) (J values in Hz). MS spectra were recorded on a VG 7070E instrument or a Finnigan MAT 90 spectrometer using *m*-nitrobenzyl alcohol (NBA) as matrix for silylated CDs and glycerol for desilylated CDs for FAB–MS experiments. Elemental analyses were carried out on a Carlo Erba EA 1108 instrument. IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer.

Fluorescence measurements

Fluorescence measurements were performed using a Perkin-Elmer LS50B luminescence spectrometer. Solutions were measured in a 1.00 cm (4 ml) or a 0.50 cm (2 ml) quartz cuvette, which was placed in a thermostatted (25.0 ± 0.1 °C) holder. Measurements at pH 7.0 were performed using an aqueous solution of KH_2PO_4 (0.1 mol dm^{-3}) which was adjusted to the required pH by addition of NaOH. For measurements at pH 1.0 a mixture of 0.05 mol dm^{-3} KH_2PO_4 and 0.05 mol dm^{-3} citric acid was used, adjusted to the required pH by addition of NaOH or HCl.

Stock solutions of the host molecule had concentrations of 1×10^{-5} or 1×10^{-6} mol dm^{-3}, depending on the experiment. To aliquots of these stock solutions, guest was added to give concentrations of 6×10^{-5} mol dm^{-3} for adamantanecarboxylic acid (ACA) and 6×10^{-3} mol dm^{-3} for cyclohexanol (CH). Higher concentrations of ACA could not be obtained due to the limited solubility of this probe. The excitation wavelengths were 305 nm at pH 1.0 and 333 nm at pH 7.0. The excitation slits were set at 2.5 nm and the emission slits at 2.5–10 nm, depending on the concentration of the probe under investigation. No oxygen quenching of the fluorescence was observed.

The titrations were carried out by starting with a solution of the host molecule (850 μl), followed by a gradual increase of the guest concentration by adding portions (at least ten) of the guest-stock solution (5–1000 μl). After every addition a new spectrum was recorded and stored in a computer. By subtracting the first from the last spectrum a differential spectrum was obtained, which revealed the wavelength at which the maximum changes in fluorescence intensity took place. At this wavelength the fluorescence intensity was determined for all spectra. This

intensity was plotted as a function of the guest concentration. Subsequently, these data were fitted with KALEIDAGRAPH 3.0.4 by Adelbeck Software asssuming a 1:1 host–guest binding equilibrium. The algorithm used can be derived as follows from the equilibrium constant (K_b) [eqn. (1)].

$$K_b = \frac{[HG]}{[H][G]} \quad (1)$$

If the total amount of host molecules $[H]_0$ is kept constant during the experiment, the concentration of host [H] and guest [G] can be written as eqns. (2) and (3), respectively.

$$[G = [G]_t - [HG] \quad (2)$$

$$[H] = [H]_0 - [HG] \quad (3)$$

In eqn. (2) the total amount of guest molecules is represented by $[G]_t$. Substitution of eqns. (2) and (3) into eqn. (1) gives, after some rewriting, eqn. (4).

$$[HG]^2 - ([H]_0 + [G]_t + K_b^{-1})[HG] + [H]_0[G]_t = 0 \quad (4)$$

Solving this equation leads to eqn. (5).

$$[HG] = \frac{([H]_0 + [G]_t + K_b^{-1}) - \{([H]_0 + [G]_t + K_b^{-1})^2 - 4[H]_0[G]_t\}^{\frac{1}{2}}}{2} \quad (5)$$

The observed fluorescence intensity is the sum of the fluorescence of the free host H and the complex HG [eqn. (6)] in which φ_H and φ_{HG} are the quantum yields for the host and the complex, respectively. Inserting eqn. (3) into (6) gives eqn. (7).

$$I = \varphi_H[H] + \varphi_{HG}[HG] \quad (6)$$

$$I = \varphi_H[H]_0 + (\varphi_{HG} - \varphi_H)[HG] \quad (7)$$

This can be seen simplified as eqn. (8), in which $[I]_0$ represents

$$I = [I]_0 + c[HG] \quad (8)$$

the initial fluorescence intensity before addition of a guest; c is a constant representing the relative difference in quantum yield between the host molecule and the complex. Finally, substitution of eqn. (5) in (8) gives the equation which describes the curve obtained from the titration experiment. All measurements were performed twice.

Fluorescence lifetimes

Fluorescence lifetimes were measured by Xavier Lauteslager at the University of Amsterdam with picosecond time correlated single photon counting using a Hamamatsu micro channel plate (R3809) detector, employing a frequency doubled DCM dye laser which was synchronously pumped with a mode locked argon ion laser resulting in 317 nm 19 ps FWHM pulses. For a more detailed description of the experimental set up see ref. 13.

Mono-3-deoxy-3-(5′-dimethylaminonaphthalene-1′-sulfonamido)-β-cyclodextrin 4

Compound **15** (121 mg, 0.056 mmol) was dried (60 °C, 1 h, 0.1 mmHg) and dissolved in 20 ml of THF. After addition of 0.5 ml of a stock solution (1 mol dm^{-3}) of TBAF (8.9 equiv.) in THF, the reaction mixture was refluxed for 24 h. After concentration *in vacuo*, the residue was dissolved in a minimum amount of ethanol–water (2:1, v/v) and the product precipitated by addition of ethyl acetate. The precipitate was collected by centrifugation. Further purification was achieved by exclusion chromatography [Fractogel TSK HW-40 (F)] (Merck), bed volume 200 ml, flow rate 13.2 ml per h, eluent water). After lyophilisation, the compound was obtained as a white solid. Yield 48 mg: (63%). Mp 270 °C (decomp.). δ_H(400 MHz; D_2O) 8.48 (d, 1 H, *H*-Ar), 8.39 (d, 1 H, *H*-Ar), 8.26 (d, 1 H, *H*-Ar), 7.71 (t, 1 H, *H*-Ar), 7.67 (t, 1 H, *H*-Ar), 7.37 (d, 1 H, *H*-Ar), 5.02, 4.98 and 4.96 (3 × d, *J* 4, 5 H, *H*-1), 4.70 (d, *J* 6, 1 H, *H*-1), 4.4 (br s, 1 H, *H*-1), 3.88–3.40 (m, 48 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6), 2.84 (s, 6 H, CH_3-N). δ_C(100 MHz; D_2O) 152.6, 136.0, 131.4, 130.8, 130.1, 129.6, 125.8, 121.9 and 117.8 (*C*-Ar), 105.0–102.4 (*C*-1), 82.7–79.8 and 76.9–71.1 (*C*-2, *C*-3, *C*-4, *C*-5), 61.7–59.3 (*C*-6), 46.7 (CH_3-N). FAB–MS (*m/z*): 1360 (M + 1). Anal. Calc. for $C_{54}H_{75}O_{36}N_2S\cdot 7H_2O$:† C, 43.64; H, 6.04; N, 1.88; S, 2.16. Found: C, 43.14; H, 6.00; N, 1.94; S, 2.27%.

Mono-2-*O*-[2′-(5″-dimethylaminonaphthalene-1″-sulfonamido)-ethyl]-β-cyclodextrin 5

Analogous to the synthesis of **4** from **15**, compound **5** was prepared from **13** (252 mg; 0.114 mmol). The product was not purified by exclusion chromatography, but subjected to cation exchange chromatography using an ion exchange column (Dowex) in the NH_4^+-form and water as the eluent. The compound was obtained as a white solid by lyophilisation of the product containing fractions. Yield 118 mg: (76%). Mp 280 °C (decomp.). δ_H[400 MHz; $(CD_3)_2SO$] 8.46 (d, 1 H, *H*-Ar), 8.27 (d, 1 H, *H*-Ar), 8.10 (d, 1 H, *H*-Ar), 7.25 (d, 1 H, *H*-Ar), 7.64 (t, 1 H, *H*-Ar), 7.60 (t, 1 H, *H*-Ar), 4.89 (d, 1 H, *H*-1), 4.81 (s, 6 H, *H*-1), 3.64–3.44 and 3.17–3.04 (2 × m, 44 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, CH_2CH_2O), 2.97 (t, 2 H, CH_2NH), 2.82 (s, 6 H, CH_3N). δ_C[100 MHz; $(CD_3)_2SO$] 151.4, 135.8, 129.5, 129.0, 128.2, 128.0, 123.8, 119.0 and 115.1 (*C*-Ar), 102.0–101.7 and 99.8 (*C*-1), 81.8–80.8 and 73.0–71.6 (*C*-2, *C*-3, *C*-4, *C*-5), 70.0 (CH_2CH_2O), 60.0–57.5 (*C*-6), 45.1 (CH_3N), 42.3 (*C*NH). FAB–MS (*m/z*): 1412 (M + 1). Anal. Calc. for $C_{56}H_{79}O_{37}N_2S\cdot 5H_2O$: C, 44.86; H, 5.94; N, 1.87; S, 2.14. Found: C, 44.56; H, 6.12; N, 1.88; S, 1.98%.

Mono-2-*O*-[8′-(5″-dimethylaminonaphthalene-1″-sulfonamido)-3′,6′-dioxaoctyl]-β-cyclodextrin 6

Compound **6** was prepared from **23** [80 mg (0.035 mmol)] in the same way as described for **5** from **13** in 79% yield (41 mg). Mp >300 °C. δ_H(400 MHz; D_2O) 8.57 (d, 1 H, *H*-Ar), 8.36 (d, 1 H, *H*-Ar), 8.30 (d, 1 H, *H*-Ar), 7.32 (d, 1 H, *H*-Ar), 7.78 (t, 1 H, *H*-Ar), 7.75 (t, 1 H, *H*-Ar), 5.11 (d, 1 H, *H*-1), 4.98–4.95 (m, 6 H, *H*-1), 3.84–3.35 (m, 54 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, CH_2O), 3.13 (br t, 2 H, CH_2NH), 2.85 (s, 6 H, CH_3N). δ_C(100 MHz; D_2O) 152.4, 135.8, 131.0, 130.6, 130.4, 130.3, 125.8, 120.7 and 116.6 (*C*-Ar), 103.3–103.0 and 101.8 (*C*-1), 83.2–81.6 and 74.6–72.2 (*C*-2, *C*-3, *C*-4, *C*-5), 70.9–69.7 (CH_2O), 61.5–61.2 (*C*-6), 46.9 (CH_3N), 43.8 (CH_2NH). FAB–MS (*m/z*): 1499 (M + 1). Anal. Calc. for $C_{60}H_{94}O_{39}N_2S\cdot 5H_2O$: C, 45.34; H, 6.55; N, 1.76; S, 2.02. Found: C, 45.37; H, 6.29; N, 1.88; S, 2.22%.

Methyl-3-deoxy-3-(5′-dimethylaminonaphthalene-1′-sulfonamido)-α-D-altropyranoside 7

This compound was prepared starting from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside, which was a kind gift of Dr Gordon Chittenden. The opening of this epoxide with ammonia was performed in an analogous way to that described by Myers *et al.*[19] to give methyl 3-amino-3-deoxy-4,6-*O*-benzylidene-α-D-altropyranoside as a crystalline product. This compound was reacted directly with dansyl chloride as follows: 196 mg (0.698 mmol) was dissolved in 25 ml of THF and 0.1 ml of triethylamine (1.03 equiv.) was added together with 176 mg (1.07 equiv.) of dansyl chloride at 0 °C. The reaction mixture was stirred for 6 h at 0 °C, followed by one

† Cyclodextrins are known to bind various amounts of crystal water, *e.g.* see ref. 2.

day at room temp. After removal of the organic solvent *in vacuo*, the residue was dissolved in ethyl acetate and the solution washed with a saturated solution of $NaHCO_3$ and with brine. The organic layer was dried over $MgSO_4$ and concentrated. Further purification was achieved by column chromatography (3% MeOH in $CHCl_3$) yielding 265 mg (74%) of the dansylated product as a yellow glass. This compound (110 mg) was directly deprotected by dissolving it in 50 ml of aqueous 0.01 mol dm^{-3} H_2SO_4 and heating at 80 °C for 4 h. Purification of the product was achieved by washing the acidic water layer with chloroform to remove the starting material and the benzaldehyde. After neutralisation of the water layer with $NaHCO_3$, the product was obtained by extraction with chloroform. After evaporation of the dried ($MgSO_4$) organic layers, the product **7** was obtained in pure form. Yield 53 mg: (58%). δ_H(90 MHz; $CDCl_3$–CD_3OD, 5:1, v/v) 8.7–8.2 (m, 3 H, *H*-Ar), 7.7–7.1 (m, 3 H, *H*-Ar), 4.4 (s, 1 H, *H*-1), 3.9–3.3 (m, 7 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6), 3.4 (s, 3 H, CH_3O), 2.9 (s, 6 H, CH_3N). EI–MS (*m/z*): 426 (M^+). Anal. Calc. for $C_{19}H_{26}O_7N_2S$: C, 53.51; H, 6.14; N, 6.57; S, 7.52. Found: C, 53.50; H, 6.28; N, 6.23; S, 6.97%.

2-Azido-ethanol 8

This compound was synthesized using a modification of a procedure described by Boyer *et al.*[20] 2-Chloroethanol (23.5 g, 0.29 mol) was added to 25.2 g (1.33 equiv.) of sodium azide and the resulting suspension was heated at 90 °C for 120 h. The reaction mixture was poured into dichloromethane (100 ml) and the sodium salts were removed by filtration. After evaporation of the dichloromethane *in vacuo* the product was purified by distillation yielding a colourless oil. Yield 12.5 g: (50%). Bp 69 °C (20 mmHg). δ_H(90 MHz; $CDCl_3$) 3.8 (t, 2 H, CH_2O), 3.3 (t, 2 H, CH_2N_3), 3.0 (s, 1 H, O*H*). ν_{max}/cm^{-1} (KBr): 2110 (N_3). CI–MS (*m/z*): 88 (M + 1), 175 (2 M + 1).

1-Tosyloxy-2-azidoethane 9

To a solution of 7.35 g (84.5 mmol) of 2-azidoethanol **8** in 50 ml of pyridine was added at 0 °C 17.96 g (1.08 equiv.) of tosyl chloride. After stirring for 24 h at room temp. the reaction mixture was concentrated *in vacuo*, the product dissolved in 75 ml of dichloromethane, and the solution washed with 1 mol dm^{-3} aqueous HCl (twice), a saturated solution of $NaHCO_3$, and brine. After drying the organic layer over $MgSO_4$ and evaporation of the solvent, the crude product was purified by column chromatography (light petroleum, bp 60–80 °C–ethyl acetate, 4:1, v/v), yielding **9** as a colourless oil. Yield 6.68 g: (32%). δ_H(100 MHz; $CDCl_3$) 7.7 (d, 2 H, *H*-Ar), 7.3 (d, 2 H, *H*-Ar), 4.1 (t, 2 H, CH_2O), 3.4 (t, 2 H, CH_2N_3), 2.4 (s, 3 H, CH_3). ν_{max}/cm^{-1} (KBr): 2105 (N_3). CI–MS (*m/z*): 242 (M + 1), 483 (2 M + 1). Anal. Calc. for $C_9H_{11}N_3O_3S$: C, 44.80; H, 4.60; N, 17.42; S, 13.29. Found: C, 44.86; H, 4.64; N, 17.08; S, 13.53%. Spectral data are in agreement with an earlier report of this compound, prepared by an alternative route in higher yield.[21]

Mono-2-*O*-(2-azidoethyl)-heptakis-6-*O*-(*tert*-butyldimethylsilyl)-β-CD 11

To a solution of 14.02 g (7.25 mmol) of dried (95 °C, 0.1 mmHg, 5 h) cyclodextrin derivative **10** in 180 ml of dry THF was added 525 mg (3.0 equiv.) of cleaned NaH. The suspension was stirred for 17 h at room temp. and 1 h at reflux temperature. Subsequently, 1.67 g (0.96 equiv.) of compound **9** was added. After 5 h of reaction, the reaction mixture was concentrated *in vacuo*, and the residue was dissolved in ethyl acetate. The solution was washed with water–brine (1:1, v/v) and dried over $MgSO_4$. After removal of the solvent *in vacuo*, 16 g of crude product was obtained which was subjected twice to column chromatography (a gradient was used going from eluent E to eluent D) to give compound **11** as a white solid. In this way also 6.2 g of pure starting material **10** was recovered. Yield of **11** 3.97 g: (27%, or 47% based on the consumed amount of **10**). Mp 253–258 °C. δ_H(400 MHz; C_6D_6) 5.32–4.93 (m, 7 H, *H*-1), 4.45–3.45 (m, 44 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, $CH_2CH_2N_3$), 3.05 (br m, 2 H, CH_2N_3), 1.35–0.80 (m, 63 H, CH_3C), 0.30–0.17 (m, 42 H, CH_3Si). δ_C(100 MHz; C_6D_6) 104.1–102.0 (*C*-1), 83.9–81.2 and 75.1–73.2 (*C*-2, *C*-3, *C*-4, *C*-5), 73.0 ($CH_2CH_2N_3$), 63.3–62.8 (C-6), 51.6 ($CH_2CH_2N_3$), 26.9 (CH_3C), 19.3 (CH_3C), −4.2 (CH_3-Si). FAB–MS (*m/z*): 2025 (M + Na) and 2135 (M + Cs). Anal. Calc. for $C_{86}H_{171}O_{35}N_3Si_7$: C, 51.55; H, 8.60; N, 2.10. Found: C, 51.63; H, 8.51; N, 2.05%.

Mono-2-*O*-(2-aminoethyl)-heptakis-6-*O*-(*tert*-butyldimethylsilyl)-β-CD 12

CD derivative **11** (300 mg, 0.152 mmol) and 12.5 mg of AIBN (0.62 equiv.) were dissolved in 6 ml of THF. After the addition of 76 mg of tri-*n*-butyltin hydride (2.1 equiv.) the reaction mixture was refluxed for 2 h. After removal of the solvent *in vacuo* the crude product was dissolved in ethyl acetate and the solution washed with water–brine (1:1, v/v) and brine. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo.* The product was obtained as a white solid after column chromatography (eluent D). Yield 220 mg: (74%). Mp 231 °C (decomp.). δ_H(400 MHz; $CDCl_3$–CD_3OD, 1:1, v/v) 4.75 (d, 1 H, *H*-1), 4.73–4.50 (m, 6 H, *H*-1), 3.75–2.75 (m, 46 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, $CH_2CH_2NH_2$), 0.58 (s, 63 H, CH_3C), −0.25 (s, 42 H, CH_3Si). δ_C(100 MHz; $CDCl_3$–CD_3OD, 1:1, v/v) 101.8–101.5 and 99.3 (*C*-1), 80.9–80.2 and 72.9–71.4 (*C*-2, *C*-3, *C*-4, *C*-5), 66.6 ($CH_2CH_2NH_2$), 61.4–61.2 (*C*-6), 38.8 ($CH_2CH_2NH_2$), 25.1 (CH_3C), 17.6 (CH_3C), −5.9 (CH_3Si). FAB–MS (*m/z*): 1978 (M + 1) and 2000 (M + Na). Anal. Calc. for $C_{86}H_{173}O_{35}NSi_7 \cdot 5H_2O$: C, 49.95; H, 8.92; N, 0.68. Found: C, 49.77; H, 8.54; N, 0.71%.

Mono-2-*O*-[2′-(5″-dimethylaminonaphthalene-1″-sulfonamido)-ethyl]heptakis-(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin 13

To a solution of 408 mg (0.21 mmol) of dried (60 °C, 0.1 mmHg, 1 h) compound **12** in 25 ml of dry THF were added 52.8 mg (0.95 equiv.) of dansyl chloride and 0.3 ml of triethylamine. After 18 h of stirring at room temp., the reaction mixture was concentrated *in vacuo*, the residue dissolved in 50 ml of ethyl acetate, and the solution washed with an aqueous saturated solution of $NaHCO_3$ (twice) and brine, and dried over $MgSO_4$. After removal of the solvent *in vacuo*, the crude product was purified by column chromatography (eluent E) to yield pure compound **13** as a white solid. Yield 263 mg: (58%). Mp >300 °C. δ_H(400 MHz; $CDCl_3$–CD_3OD, 5:1, v/v) 8.53 (d, 1 H, *H*-Ar), 8.33 (d, 1 H, *H*-Ar), 8.21 (d, 1 H, *H*-Ar), 7.20 (d, 1 H, *H*-Ar), 7.60 (t, 1 H, *H*-Ar), 7.53 (t, 1 H, *H*-Ar), 4.94 (m, 7 H, *H*-1), 3.99–3.48 (m, 46 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, CH_2CH_2NH), 3.14 (t, 2 H, CH_2CH_2NH), 2.89 (s, 6 H, CH_3N), 1.04–0.73 (s, 63 H, CH_3C), 0.08–0.00 (s, 42 H, CH_3Si). δ_C(100 MHz; $CDCl_3$–CD_3OD, 5:1, v/v) 151.5, 135.1, 130.0, 129.7, 129.45, 128.7, 128.1, 123.0, 119.1 and 115.1 (*C*-Ar), 102.4–102.0 and 99.4 (*C*-1), 81.7–80.6 and 73.2–71.8 (*C*-2, *C*-3, *C*-4, *C*-5), 70.9 (CH_2CH_2NH), 61.5 (*C*-6), 45.2 (CH_3N), 42.6 (CH_2CH_2NH), 25.6–25.5 (CH_3C), 18.1 (CH_3C), −5.4 to −5.5 (CH_3Si). FAB–MS (*m/z*): 2232 (M + Na). Anal. Calc. $C_{98}H_{184}O_{37}N_2SSi_7 \cdot 2H_2O$: C, 52.33; H, 8.37; N, 1.25; S, 1.42. Found: C, 52.07; H, 8.22; N, 1.21; S, 1.50%.

Mono-3-deoxy-3-(5′-dimethylaminonaphthalene-1′-sulfonamido)heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin 15

Compound **14**, 203 mg (0.092 mmol), was dried (60 °C, 0.5 mmHg, 1 h) and dissolved in 15 ml of dry THF. To this solution was added 23.6 mg (0.95 equiv.) of dansyl chloride and 0.02 ml of triethylamine at 0 °C. After 10 h the reaction mixture was allowed to warm to room temp. and was stirred for an additional 24 h. The reaction mixture was concentrated *in vacuo*, the residue dissolved in 50 ml of ethyl acetate, and the solution washed with a saturated solution of $NaHCO_3$ (twice), and brine and subsequently dried over $MgSO_4$. After removal of the

solvent *in vacuo*, the crude product was subjected to column chromatography (eluent A) to yield compound **15** as a slightly yellow solid. Yield 127 mg: (59%). This compound was directly desilylated and characterised only by FAB–MS. FAB–MS (*m*/*z*): 2182 (M + Na).

8-Tosyloxy-3,6-dioxaoctanol 17

To a suspension of 4.34 g of cleaned sodium hydride (110 mmol) in 750 ml of THF was added 150 g of triethylene glycol (100 mmol). After gas evolution had stopped, a solution of 19.06 g of tosyl chloride (100 mmol) in 20 ml of THF was added in 15 min. After 18 h the mixture was concentrated *in vacuo* and the residue dissolved in 250 ml of ethyl acetate. This solution was washed with water and brine, dried over $MgSO_4$, and concentrated to give a colourless oil. Yield 24.33 g: (80%). δ_H(90 MHz; $CDCl_3$) 7.8 (d, 2 H, *H*-Ar), 7.4 (d, 2 H, *H*-Ar), 4.1 (t, 2 H, CH_2OTs), 3.7–3.5 (m, 10 H, CH_2O), 2.4 (s, 3 H, CH_3-Ar). EI–MS (*m*/*z*): 305 (M + 1). Spectral data are consistent with an earlier report of this compound, which was prepared in a different manner with comparable yield.[22]

1,1,1-Triphenyl-10-tosyloxy-2,5,8-trioxadecane 18

Compound **17** (15 g, 50 mmol) was dissolved in 300 ml of THF and 5 ml of pyridine and 13.7 g of triphenylmethyl chloride were added. After 20 h of refluxing the mixture was concentrated *in vacuo*. The residue was dissolved in ethyl acetate, washed with water and brine, dried over $MgSO_4$, and concentrated. The crude product was purified by column chromatography (ethyl acetate–hexane, 1:9, v/v), yielding **18** (11 g) as a yellow oil in 40% yield. δ_H(90 MHz; $CDCl_3$) 7.7 (d, 2 H, *H*-Ar), 7.5–7.0 (m, 17 H, *H*-Ar), 4.1 (t, 2 H, CH_2-OTs), 3.7–3.5 (m, 8 H, CH_2-O), 3.2 (t, 2 H, CH_2-OTrt), 2.4 (s, 3 H, CH_3-Ar). Spectral data are in agreement with an earlier report of this compound, prepared in a different manner.[23]

1,1,1-Triphenyl-10-amino-2,5,8-trioxadecane 19

Ethanol (250 ml) was saturated with ammonia gas at 0 °C by bubbling for 30 min. After addition of 1.0 g (1.83 mmol) of compound **18**, the reaction mixture was transferred to an autoclave and heated for 15 h at 80 °C. It was subsequently concentrated *in vacuo* and dissolved in ethyl acetate. The solution was washed with water and brine and dried over $MgSO_4$. After removal of the solvent, compound **19** was obtained as a light-orange oil. Yield 512 mg: (72%). δ_H(90 MHz; $CDCl_3$) 7.5–7.1 (m, 15 H, *H*-Ar), 4.5 (s, 2 H, NH_2), 3.7–3.5 (m, 10 H, CH_2O, CH_2NH_2), 3.2 (t, 2 H, CH_2OTrt).

1,1,1-Triphenyl-10-(5′-dimethylaminonaphthalene-1′-sulfonamido)-2,5,8-trioxadecane 20

To a solution of 492 mg (1.26 mmol) of compound **19** in 50 ml of THF and 0.2 ml of triethylamine (1.1 equiv.) was added 380 mg (1.1 equiv.) of dansyl chloride. This mixture was stirred for 6 h and concentrated *in vacuo*. The residue was dissolved in ethyl acetate and the solution washed with water and brine and dried over $MgSO_4$. After removal of the solvent, the crude product was purified by column chromatography (ethyl acetate–hexane 1:9, v/v), which yielded compound **20** as a yellow viscous oil. Yield 389 mg: (49%). δ_H(90 MHz; $CDCl_3$) 8.6–8.1, 7.5–7.4 and 7.3–7.1 (3 × m, 21 H, *H*-Ar), 3.7–3.0 (m, 12 H, CH_2O), 2.8 (s, 6 H, CH_3N). EI–MS (*m*/*z*): 624 (M^+).

8-(5′-Dimethylaminonaphthalene-1′-sulfonamido)-3,6-dioxaoctanol 21

Compound **20** (352 mg, 0.56 mmol) was dissolved in 25 ml of dichloromethane and 1.6 g (20 equiv.) of $ZnCl_2$ was added. Dry methanol was added to obtain a homogeneous system. After 20 h of stirring at room temp., the reaction mixture was concentrated *in vacuo* and the residue dissolved in 50 ml of ethyl acetate. The resulting solution was washed with water and brine, dried over $MgSO_4$, filtered and rotary evaporated. The crude product was purified by column chromatography (ethyl acetate–hexane, 2:1, v/v) yielding compound **21** as a yellow oil. Yield 171 mg: (72%). δ_H(90 MHz; $CDCl_3$) 8.6–8.1, 7.7–7.4 and 7.3–7.1 (3 × m, 6 H, *H*-Ar), 3.8–3.4 (m, 12 H, CH_2O), 3.2 (t, 2 H, CH_2NH), 2.8 (s, 6 H, CH_3N), 1.7 (br s, 2 H, N*H*, OH). EI–MS (*m*/*z*): 382 (M^+).

8-(5′-Dimethylaminonaphthalene-1′-sulfonamido)-1-tosyloxy-3,6-dioxaoctane 22

A mixture of 148 mg of **21** (0.44 mmol) and 96 mg of tosyl chloride (1.1 equiv.) in 25 ml of pyridine was stirred for 20 h. Another portion of tosyl chloride (50 mg) was added and the reaction mixture stirred for an additional 18 h. After concentration *in vacuo*, the residue was dissolved in 50 ml of dichloromethane and the resulting solution was washed with 1 mol dm^{-3} HCl, a saturated solution of $NaHCO_3$ and brine. After drying over $MgSO_4$, and evaporation of the solvent, the crude product was purified by column chromatography (10% MeOH in $CHCl_3$) which afforded **22** as a yellow oil. Yield 159 mg: (66%). δ_H(90 MHz; $CDCl_3$) 8.6–8.1, 7.1–7.0 (2 × m, 10 H, *H*-Ar), 4.1 (t, 2 H, CH_2OTs), 3.6 (t, 2 H, CH_2CH_2OTs), 3.5–3.4 (m, 6 H, CH_2O), 3.1 (t, 2 H, CH_2NH), 2.8 (s, 6 H, CH_3N), 2.3 (s, 3 H, CH_3-Ar). EI–MS (*m*/*z*): 536 (M^+).

Mono-2-*O*-[8′-(5″-dimethylaminonaphthalene-1″-sulfonamido)-3′,6′-dioxaoctyl]heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin 23

To a solution of 485 mg (0.25 mmol) of dried (100 °C, 0.5 mmHg, 5 h) compound **10** in 25 ml of dry THF was added NaH (60% dispersion in mineral oil, 25 mg, 2.5 equiv.). The solution was stirred for 17 h at room temp. and 1 h at reflux. Subsequently, 73.5 mg (0.56 equiv.) of compound **22** was added. After 24 h refluxing, the reaction mixture was concentrated *in vacuo*, the residue dissolved in ethyl acetate and the resulting solution washed with water and brine and dried over $MgSO_4$. After removal of the solvent *in vacuo*, the crude product was purified by column chromatography (eluent B) to yield pure compound **23** as a light yellow solid. Yield 104 mg: (33%). Mp >300 °C. δ_H(400 MHz; $CDCl_3$–CD_3OD, 7:1, v/v) 8.54 (d, 1 H, *H*-Ar), 8.34 (d, 1 H, *H*-Ar), 8.23 (d, 1 H, *H*-Ar), 7.21 (d, 1 H, *H*-Ar), 7.52 (m, 2 H, *H*-Ar), 5.00 (d, 6 H, *H*-1), 4.94 (s, 1 H, *H*-1), 4.01–3.38 (m, 58 H, *H*-2, *H*-3, *H*-4, *H*-5, *H*-6, CH_2-O), 3.14 (t, 2 H, CH_2NH), 2.90 (s, 6 H, CH_3N), 1.04–0.73 (s, 63 H, CH_3C), 0.08–0.00 (s, 42 H, CH_3Si). δ_C(100 MHz; $CDCl_3$–CD_3OD, 7:1, v/v) 151.5, 135.2, 129.9, 129.6, 129.4, 128.7, 127.1, 123.0, 118.9 and 115.0 (*C*-Ar), 102.0–101.7 and 100.4 (*C*-1), 81.9–80.1 and 73.2–72.0 (*C*-2, *C*-3, *C*-4, *C*-5), 71.1–69.1 (CH_2O), 61.7–61.3 (*C*-6), 45.1 (CH_3N), 42.4 (CH_2NH), 25.5–25.4 (CH_3C), 18.0 (CH_3C), −5.5 (CH_3Si). FAB–MS (*m*/*z*): 2322 (M + Na). Anal. Calc. for $C_{102}H_{192}O_{39}N_2SSi_7 \cdot 1H_2O$: C, 52.90; H, 8.38; N, 1.21; S. 1.38. Found: C, 52.88; H, 8.76; N, 1.24; S, 1.10%.

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